MONOAMINE METABOLISM IN THE STRIATUM OF THE RAT BRAIN DURING DRUG INFUSION INTO THE NUCLEUS ACCUMBENS

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Studies on conscious Sprague-Dawley rats using intracerebral dialysis in live animals combined with high-performance liquid chromatography with electrochemical detection showed that administration of apomorphine into the nucleus accumbens decreased the levels of dihydroxyphenylacetic acid and 5-hydroxyindoleacetic acid in the extracellular space of the dorsal striatum throughout the observation period and produced a transient reduction in the level of homovanillic acid in the dialysate from this structure. The studies demonstrated that reversible exclusion of the nucleus accumbens with procaine produced a transient increase in the levels of dopamine metabolites, without an increase in serotonin metabolites, in the extracellular space of the dorsal striatum. These results demonstrate that the nucleus accumbens affects dopamine metabolism in the striatum, this being mediated by the dopamine-reactive system in the nucleus accumbens.

Key words: Microdialysis, dopamine, nucleus accumbens, striatum.

The nucleus accumbens and striatum are related structures of the forebrain with parallel involvement in organizing mutually complementary forms of motor behavior [4], which suggests the existence of mechanisms coordinating the functions of these structures. One of the most important mechanisms for coordinating the functions of these nuclei could consist of interactions between their monoaminergic systems, whose functions are associated with regulating the functional activity level of these structures. We have previously demonstrated in ex vivo studies that tissue dopamine metabolism is activated in the striatum when dopaminergic terminals of the nucleus accumbens in rats are damaged by the neurotoxin 6-hydroxydopamine [1]. Subsequently, studies using intracerebral dialysis in live animals combined with radioenzyme analysis of dopamine levels showed that administration of phenamine into the nucleus accumbens decreased, while administration of haloperidol and tetrodotoxin increased the extracellular dopamine concentration in the dorsal striatum [2]. These points led to the suggestion that the nucleus accumbens has tonic inhibitory influences on the dopaminergic system of the striatum, which is controlled by the dopaminergic input of the nucleus accumbens and which has the function of coordinating the operations of these subcortical structures [2]. However, knowledge of the pattern of interactions of these two structures remains incomplete without data on changes in dopamine metabolite concentrations in the extracellular space of the dorsal striatum in living animals during exposure to pharmacological intervention into the nucleus accumbens. Additionally, the literature completely lacks data on the effects of the nucleus accumbens on the other monoaminergic system which innervates the striatum, i.e., the serotonergic system.

The aim of the present work was to study changes in the extracellular contents of dopamine and serotonin metabolites in the dorsal striatum during modification of the dopamine-reactive system of the nucleus accumbens with apomorphine and during reversible exclusion of this structure with procaine.

METHODS

Studies were carried out on 20 male Sprague-Dawley rats weighing 250-300 g. Under hexenal anesthesia, U-shaped dialysis cannulae were implanted unilaterally in the dorsal striatum and the nucleus accumbens; cannulae were prepared in the Laboratory for the Physiology of Higher Nervous Activity, I. P. Pavlov Institute of Physiology, Russian Academy of Sciences, 199034 St. Petersburg. Translated from Fiziologicheskii Zhurnal imeni I. M. Sechenova, Vol. 82, No. 2, pp. 13-19, February, 1996. Original article submitted December 27, 1994.
laboratory using dialysis membrane with an exclusion limit of 5000 Dal (GAMBRO, Germany). The length of the working part was 3 mm in the striatum and 2 mm in the nucleus accumbens (Fig. 1). Implantation site coordinates were as follows: striatum: 0.5 mm dorsal to the bregma, 2.5 mm lateral to the midline, and 6 mm in depth from the surface of the skull; nucleus accumbens: 2.5 mm rostral to the bregma, 1.2 mm lateral to the sagittal suture, and 8 mm in depth from the surface of the skull. One day after surgery, each rat was placed into the experimental chamber, and dialysis cannulae were attached to a perfusion pump which was used for dialysis perfusion of the nucleus accumbens and striatum at a rate of 2 μl/min with artificial CSF [2] throughout the experiment. Striatum dialysate was collected every 15 min and was analyzed immediately for acidic dopamine metabolites (dihydroxyphenylacetic and homovanillic acids) and for the serotonin metabolite 5-hydroxyindoleacetic acid. Dialysate from the nucleus accumbens was frozen immediately after collection and was stored at -10°C for no more than 5 h before analysis, without addition of any stabilizer. When the baseline had stabilized (usually in 60-90 min), four background portions of dialysate were collected, after which animals were divided into groups. Apomorphine was added to the artificial CSF used as the dialysis perfusate for the nucleus accumbens of rats of group 1 (n = 6), at a concentration of 20 μM, while procaine (10 μM) was added for group 2 (n = 6). All agents were obtained from Sigma (USA). Animals of control group 4 (n = 8) received CSF of constant composition throughout the experiment. A further four portions of dialysate were collected at this point. Apomorphine (20 μM) was then added to the procaine-containing CSF used for perfusion of the nucleus accumbens of group 2 animals, to address the question of possible diffusion of apomorphine from the dosage site in the nucleus accumbens to the region of the dorsal striatum. A further four dialysate fractions were then collected. Monoamine metabolite contents in dialysate portions were determined by HPLC using a BAS LC-4B (USA) electrochemical detector. An electrochemical cell of Russian origin was used, from Diagnostikum, Moscow. The carbon glass working electrode was maintained at a potential of +0.75 V relative to the Ag/AgCl reference electrode. The stationary phase consisted of a reverse-phase chromatography column of length 150 mm and internal diameter 3 mm filled with Separon C18 (5 μm), ChSR, from Diagnostikum, Moscow. The mobile phase contained 0.175 M CH3COOH, 0.05 M CH3COONa.3H2O, 0.27 M EDTA, 0.875 M sodium octylsulfonate, and 1.25% acetonitrile, and the pH was 3.6. The flow rate was 0.7 ml/min, the pressure was about